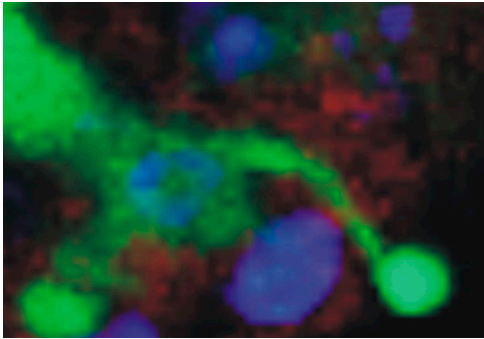


Dynamic DCs of the gut



Dendritic cells (green) reach their finger-like protrusions past the gut epithelia to catch bacteria.

Dendritic cells (DCs) stretch finger-like extensions into the gut to capture bacteria. But, according to Chieppa et al. ([page 2841](#)), it is the gut epithelial cells that first recognize the bacteria and then give DCs the tip-off.

Regular sampling of gut bacterial antigens by the immune system is necessary for maintaining tolerance to commensal bacteria and for defending against pathogens. DCs gather bacterial antigens using their extensions, but Chieppa et al. show that these extensions are not a constitutive feature of gut DCs.

Treatment of mice with antibiotics reduced the number of DC extensions in the small bowel, whereas oral infection of mice with *Salmonella* increased their numbers. DC extensions are thus dependent on the presence of the bacteria themselves. Indeed, live imaging using intravital microscopy showed that DC extensions begin to emerge from the gut wall following bacterial exposure and remain protruded for 10–40 min before retracting with their quarry.

Recognition of bacteria by innate immune cells is often dependent on Toll-like receptors (TLRs). Recent studies reveal that gut epithelial cells also have TLRs, and the group show here that mice lacking specific epithelial but not DC TLRs failed to extend DC processes across their gut wall in response to the relevant bacterial stimuli. Although the team does not yet know how epithelial cells alert the DCs, the gut barrier function of the epithelial cells makes them the perfect choice to be the first to perform identity checks on gut bacteria. [JEM](#)

Get Syk and get cycling

Rampant proliferation of pre-B cells in leukemia can be caused by overly active proto-oncogenes such as c-Myc. Wossning et al. ([page 2829](#)) now discover that this c-Myc surplus is driven by a tyrosine kinase called Syk. But even with lots of c-Myc, pre-B cells still need Syk to cycle.

B cell proliferation and differentiation must be tightly controlled to avoid the release of immature, nonfunctional cells into the circulation. The proliferation is driven by the pre-B cell receptor (pre-BCR), which activates Syk. Syk's role in proliferation is murky: it is overexpressed in some types of lymphoma and leukemia cells, yet it activates a known tumor suppressor and is down-regulated in certain malignant cancers.

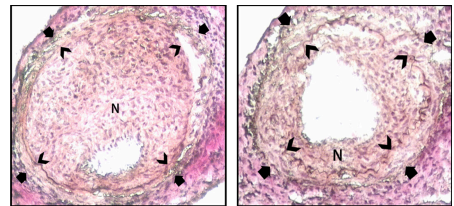
To sort through this confusion, Wossning et al. overexpressed Syk in pre-B cells, which transformed the cells into an overproliferative, undifferentiated state. A Syk-specific inhibitor reversed this phenotype. The team thus concludes that Syk is a proto-oncogene rather than tumor suppressor, at least in this cell type.

The group also found that Syk promoted c-Myc expression. The addition of more c-Myc was all that was needed to transform pre-B cells, yet this transformation was reversed by Syk inhibition. Furthermore, c-Myc expression did not transform pre-B cells that lacked the pre-BCR. Together, these results indicate that Syk must be turning on other necessary proliferative or survival signals—perhaps Bcl-2 family members—in addition to c-Myc.

The finding that transformation resulting from either too much Syk or too much c-Myc can both be blocked with a Syk inhibitor suggests that a variety of B cell proliferative disorders might respond to this type of treatment. [JEM](#)

FSAP reduces risk of repair

Overenthusiastic repair of damaged blood vessels could cause a fatal blockage. Sedding et al. ([page 2801](#)) report that the normal repair-restricting function of factor VII activating protease (FSAP) is disrupted by a common mutation. People carrying the mutation might thus be more at risk of vessel narrowing.



After vascular injury, repair is restricted in the presence of FSAP (right) to prevent narrowing of the blood vessel.

Approximately 5% of the population carries an FSAP polymorphism linked to cardiovascular disease. The authors' previous in vitro evidence suggested that wild-type FSAP, a plasma protein, limits vessel repair processes in part by inactivating PDGF-BB—a growth factor which promotes the proliferation and migration of blood vessel wall cells during repair.

The team isolated and characterized the mutated form of FSAP and discovered that although its ability to bind PDGF-BB was unaltered, it failed to cleave the protein efficiently. Wild-type human FSAP reduced vascular cell proliferation and accumulation at sites of injury in a mouse model—most likely by reducing PDGF-BB activity. The mutant protein, however, provided no such restraint, suggesting that people possessing the mutation might generate excessive scar tissue during vessel repair.

Vessel narrowing occasionally recurs after surgical repair. If, as the team suspects, recurrence correlates with the FSAP polymorphism, then screening cardiovascular patients for the mutation might identify those at risk. [JEM](#)